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ORIGINAL ARTICLE

Snake Envenomation in the Intensive Care Unit of a Tertiary Care Hospital, Dhaka, Bangladesh: A Prospective Cohort Study

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Abstract

Background: Snake bite and the subsequent envenomation is an important health hazard which may lead to fatality in rural areas of Bangladesh. **Objective:** This study was conducted to evaluate the epidemiology, clinical profile, treatment and outcome for patients with snake bite admitted in the intensive care unit of Dhaka Medical College Hospital, Bangladesh. **Methodology:** This prospective cohort study was conducted in the Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine, Dhaka Medical College, Dhaka, Bangladesh from May 2019 to April 2020 for a period one year. The patients of snake bite were treated in the Intensive care unit, Dhaka Medical College Hospital, Dhaka, Bangladesh. A questionnaire, containing information on bite, physical examination and identification of snake was used. **Results:** A total number of 23 patients of snake bite were treated in the Intensive care unit. Among the patients, 16 (69.56%) were bitten by cobra, 2 (8.6%) were suspected to be bitten by krait and 5(21.7%) cases had Russel viper bite. Tight tourniquet was used in 15(65.21%) cases. Among the patients 18(78.26%) patients were observed with the features of neurotoxicity with or without local envenoming. Among all patients, one patient required two doses of ASV, another patient needed 3 doses; but the other patients were found to be improved after getting a single dose of ASV. However, 15 patients needed ventilator support. The mean duration of ventilator support was 4.8 days. The mortality was 30.43% (7 patients). Out of these 7 patients, 4 patients died due to acute renal failure with DIC. **Conclusion:** Neuroparalytic Cobra envenomation is accounted for the highest incidence of venomous bites in the present study. [*Journal of Current and Advance Medical Research, January 2022;9(1):48-55*]

Keywords: Snake bite; reptile; snake envenomation; ICU management

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Introduction

Snake bite is one of the significant causes of global morbidity and mortality. It has been estimated that 5 million snake bite cases occur worldwide every year, causing about 100,000 deaths[1]. Globally snakebites (envenoming) incidence has been estimated as 500,000 and mortality in 30000 to 40000 cases per year[2]. Chippaiux[3] estimated that venomous snakes cause 5.4 million bites, approximately 2.5 million envenomings and over 125,000 deaths worldwide annually[3]. An epidemiological study estimated the incidence of snake bites in Bangladesh about 8000 per year with 22% mortality which has been identified to be one of the highest in the world[4]. Bangladesh supports approximately 80 species of snakes[5-6]. The true incidence of snake bite in rural Bangladesh is largely unknown. An incidence of 4.3 snake bites per 100,000 populations was reported with approximately 2000 deaths occurring annually in Bangladesh[7]. During 1988 to 89, a small survey was conducted in 50 Upazilla (sub-districts) of Bangladesh that recorded 764 episodes of snakebite of which 168 (22%) died[8]. According to Faiz et al[9], 1666 snake bite victims attended to the Chittagong Medical College Hospital (CMCH) for treatment between 1993 and 2003. Among those victims, 28.5% were bitten by poisonous snakes and only eight (0.5%) died. During the flood of 2004 DGHS recorded 99 death following snake bite through the existing surveillance system[10] .This is known to be a health hazard for centuries which has under the per-view of traditional healers, 'Ohzas' who used to demonstrate a number of rituals for providing treatment which have been found to be useless, at times harmful[11].

Snake bite is a result of an unfortunate accidental interaction between a snake and a human victim. Among the snake families, two major families of snakes account for most venomous snakes dangerous to humans. These are family Elapidae and the Viperidae. Among the Elapidae, cobra bite usually causes neurotoxic features with local envenoming. Other Elapidae like krait bites usually causes neurotoxic features without local envenoming. Among the Viperidae, Russell's viper bites usually causes local envenoming with heamatological manifestations rarely with neurotoxicity whereas the green pitbites cause local envenoming with hematological toxicity. Sea snake bites usually causes myotoxicity. Serious venom effects can be delayed for hours. A victim who initially appears well could still become quite sick. All victims should seek medical care without delay[12-16].

Appropriate first aid includes immobilization of the bitten limb, non-tempering the bite site and quick referral for evaluation for envenomation[17]. Hospital management includes differentiation of venomous from non-venomous bite by looking for clinical criteria, bed site 20 minute whole blood clotting test, species identification by careful examination of brought specimen[18]. In Bangladesh, method for detection of venom-antigen is not available for routine clinical practice. Based on clinical criteria of envenomation polyvalent anti snake venom, the specific drug for treatment of venomous snake bite is provided depending on availability[11].

The anti-snake venom (ASV) is not manufactured in Bangladesh and the supply is being given in government hospital which is manufactured in India in either lyophilized or in serum form[19]. The supply of ASV in public hospital is irregular and is not available in private hospitals and is not easily available in the private market as well. Being a rural poor man's life threatening health condition, snake bite deserves special attention for saving young active earning members of the community conforming our pro-poor strategy and commitment of Millennium Development Goal. There is scanty information about snake bite from Bangladesh and published reports are mostly from Chittagong, Khulna, Rajshahi and Dhaka though snake bite cases are not uncommon but there was no published report from the intensive care unit, Dhaka Medical College Hospital, the biggest tertiary care public hospital of the country except a case report and a study from the department of medicine[13-14]. As the snake bite cases and death due to the neurotoxicity is a medical emergency issue, studies are required to understand in perspective of snake species, modes of the snake bites; signs, symptoms and treatments in different age-sex groups of people in Bangladesh are demanded. This present study was undertaken to see the demographic profile- age sex, occupation, time of bite site, site of bite, pre hospital management, ICU management, mechanical ventilatory support, duration of mechanical ventilation and to see the outcome of the cases of snake bite.

Methodology

This prospective cohort study was carried out at a teaching hospital Dhaka Medical College Hospital, Dkaka, Bangladesh after the approval of the Institutional Ethical Committee. This is a multidisciplinary tertiary hospital in the capital of Bangladesh. In this study, those patients were included whom admitted in the ICU with complains of snake bite. The records data of patients were

obtained after admission in the intensive care unit from May 2019 to April 2020 for period of one year. Patients meeting the following criteria were included in our study like definitive history of snake bite with or without presence of fang marks, the presence of acute onset neuroparalytic symptoms with a history of snake bite or presence of fang marks and the presence of local signs like swelling, inflammation, bleeding from the site with a history of snake bite or presence of fang marks. Patients with non-venomous snake bites and ambiguous history were excluded from the study. Patients who did not exhibit signs and symptoms of snake bite after a period of observation of 24 hours were labeled as non-venomous. Clinical envenomation was defined by presence of signs and symptoms of local or systemic toxicity. Local signs were the presence of fang marks, bleeding, swelling or necrosis. Systemic toxicity was defined as presence of neuroparalytic features or hemostatic abnormalities. Data were collected from the patients/attendants and medical record during the period of hospital stay. The demographic profile, time, site, date and time of biting, clinical features, time interval elapsed between the bite and medical treatment including administration of anti-snake venom (ASV), the dosage of ASV, adverse reactions to ASV, administration of anticholinesterase, indication for mechanical ventilation, duration of mechanical ventilation, complications and clinical outcomes were recorded. Laboratory results of hemoglobin, total leucocyte count, platelet count, serum creatinine, blood urea, serum alanine aminotransferase and aspartate aminotransferase, alkaline phosphatase, arterial blood gas analysis of patients with respiratory difficulty were recorded. Urine routine microscopy, prothrombin time, International Normalized Ratio (INR) and 20 min whole blood clotting test and electrocardiography were recorded. The complications, survival and mortality were also recorded. Neurotoxicity was defined as presence of ptosis, ophthalmoplegia, weakness of the muscles of extremities, difficulty in breathing and inability to lift the head. Hemolytic toxicity was defined as deranged 20 min whole blood clotting test (WBCT) or the presence of spontaneous visible bleeding signs. Hypotension was defined as systolic blood pressure lower than 90 mm Hg. Oliguria was defined as urine output lower than 0.5 mL/kg/h. Serum fibrinogen levels, fibrin degradation products and D-dimers levels were not uniformly available in this hospital during the period of my prospective observational study. Disseminated intravascular coagulation was therefore defined by a deranged 20 min WBCT, deranged prothrombin time and International Normalized Ratio. This study was approved by the institutional review board (IRB) of this hospital. Statistical analyses was performed with SPSS software, versions 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Continuous data were summarized in terms of the mean, standard deviation, minimum, maximum and number of observations. Categorical or discrete data were summarized in terms of frequency counts and percentages.

Results

A total number of 23 cases with venomous bite were admitted in ICU. Among the venomous bites 16 cases were by suspected cobra and 2 cases were by suspected krait and 5 cases were suspected Russel's Viper. Among the patients 18 patients were presented with features of neurotoxicity with or without local envenoming and 5 patients were presented with haematological manifestation. All the patients were managed by ASV and other supportive treatment. Among the patients 65.21% cases were male and 34.78% cases were female. The age of the victims were varied from 10 years to 70 years with a mean of 36.17 years (Table 1).

Table 1: Age Distribution of Patients (n=23)

Age Group	Frequency	Percent
0 to 10 Years	1	4.34
11 to 20 Years	3	13.04
21 to 30 Years	3	13.04
31 to 40 Years	8	34.78
41 to 50 Years	5	21.73
51 to 60 Years	2	8.60
61 to 70 Years	1	4.34
Total	**23**	**100.0**

Mean age±SD=36.17±12.56 years

Out of 23 enrolled patients 91% were from rural areas and majorities were farmers. Figure I illustrates various states of the patients i.e., the time, season, circumstances and sites of snakebite; the treatments they have been given before and the channels they came to ICU. Out of the 23 studied patients, 15 were given mechanical ventilation as they required and the rests were not. The mean duration of ventilator support was 4.8 days; the duration of mechanical ventilation for different number of patients are shown in Figure I(f) and out of the patients, 7 (23.43%) died and 16 (69.57%) survived.

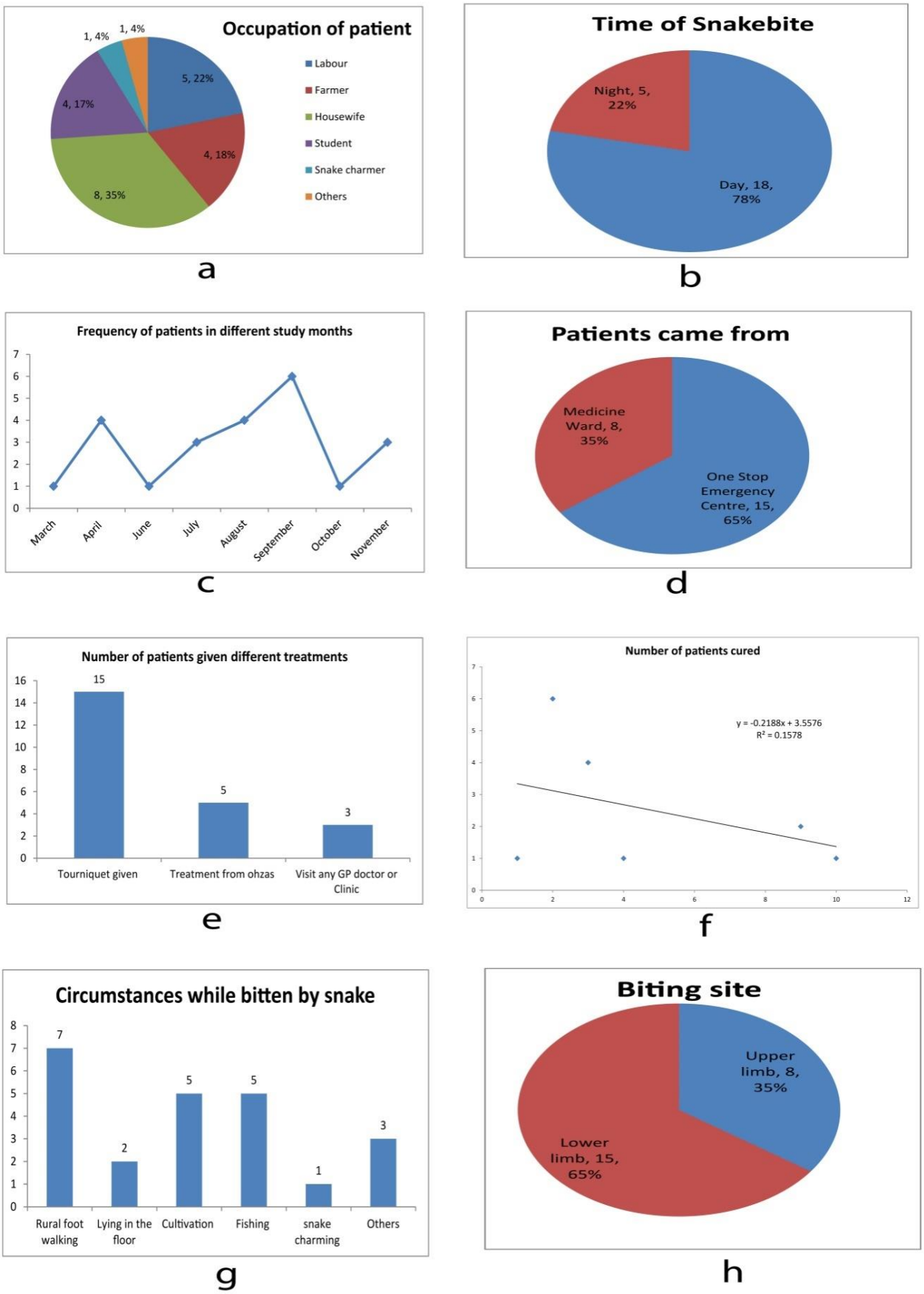

Figure I: Socioeconomic and treatment factors of the patients- a) Occupation of the patients, b) time of snakebite, c) Number of patients in different study months, d) Patients came from two different channels to ICU, e) The patterns of treatments given to the snake victims before, f) The number of patients who required mechanical ventilation (x-axis shows the days they require ventilation and y-axis reveals the number of patients), g) The circumstances of patients while being bitten, and; h) the snake biting site of the victim's body.

Table 2: Clinical Manifestations of Patients (n=23)

Clinical Feature	Frequency	Percent
Ptosis	18	78.26
Double vision	16	69.56
Muscle weakness/ Broken neck sign	15	65.21
Difficulty of breathing	15	65.21
Difficulty of deglutition	8	34.78
Slurring of speech	6	26.08
Aphasia	4	17.39
Local signs	5	21.73
Epistaxis	4	13.04

Among the patients 1 patient required two dose of ASV, 1 patient 3 dose but other patients improved by one dose of ASV. Eight patients required inotropic support during the course of ICU stay. Five patients developed oliguria and progressed to acute renal failure requiring dialysis and four patients developed disseminated intravascular coagulation (DIC). Three patients required platelet transfusion and five required fresh frozen plasma transfusion in the intensive care unit. Three patients had cardiac arrests while transferring to ICU, CPR given but developed Hypoxic Brain Injury. The mortality was 30.43% (7 patients). Out of these 7 patients, 4 died due to acute renal failure with DIC. Three patients who were referred from medicine ward, cardiac arrest occurred while transferring to ICU and develop Hypoxic Brain Injury, deteriorated further in the ICU and died (Table 3).

Table 3: Complications due to Snake Bite (n= 23)

Complications	Frequency	Percent
Local envenomation	3	13.04
Neurological Involvement	18	78.26
Hemostatic Abnormality	5	21.73
Cardiovascular Abnormality	2	8.60
Acute Renal failure	5	21.73
Hypoxic brain injury	3	13.04
DIC	4	17.39

DIC=Disseminated Intravascular coagulation

Discussion

In this study it has been evaluated the epidemiology of snake bite envenomation, clinical features, treatment, complications and outcome of patients admitted to the intensive care unit of a tertiary care hospital in Dhaka Bangladesh. Majority of patients are in the age group of 31 to 40 years (36.17%). Patients in this age group are belonged to the working class, and are mainly involved in outdoor activities. This observation is comparable with another hospital based study conducted in northern Bangladesh on 68 cases where the mean age was 26.7 years[10]. Study conducted in Chittagong Medical College Hospital found mean age of 29.6% cases[20]. Study in Nepal reported 85.0% victims were less than 45 years old[17]. Male predominance in this series is similar to other studies in Chittagong, Rajshahi and Khulna[13,18-24]. Majority of the victims are farmers which corresponds to a long-term study in Pune, India[20].

The highest number of bites occurred during daytime in this present study which is similar to other studies in Bangladesh[10,12,20]. As most of the snake bites are occurred by accidental interaction so occupational activities by rural people during the day time is the reason of increased number of bites. However in a Sri Lankan study[21] and an Indian study[25] have revealed midnight predominance. Lower limb is the most common site of bite in this study which is supported by other studies in home and abroad[10,14,19,20-34]. Most of the snake bites happened between May to October in this present series as well as in other studies[14,18,19,25,29,34]. We also observed similar trends with an increased incidence in the monsoon months.

A significant number of patients used tight tourniquet which is far from scientific and safety. It is recommended that application of tourniquet over a single bone for a brief period could be used as a first aid measure to prevent and delay the spread of venom in the systemic circulation. Tun Pe et al. demonstrated that application of local pressure by compression pad and immobilization of the limb could retard the venom antigenaemia in 13 of the 15 cases[23]. A large number of victims received pre-hospital treatment from Ohzas (traditional healers). The mode of treatment by Ohzas were in the form of multiple incisions, cauterization by chemicals, suction by mouth, ingestion of oil, ghee, herbal products.

A study in northern Bangladesh showed 7 deaths(26%) treated with antivenom in a dose of 20 ml to 40 ml. Study of Khulna Medical College shows that out of 108 venomous snake bite cases 101(93.52%) recovered completely and 7(6.66%) died after admission and 60(55.5%) cases recovered with 20-30 ml(2-3 vials) of polyvalent antisnake venom[19]. A prospective study of hospital practice in the Gampaha district,Sri Lanka including 466

patients of whom 184 patients were venomous bite showed only 2 patients were dead(0.43%) where at least 10 vials (100ml) of antivenom was initially given[24].

Snake bite poisoning caused by the cobra and krait predominantly affects the neurological system. The clinical manifestations of cobra and krait bite include paralysis of the ocular, bulbar and limb girdle muscles. It is reported that ptosis is the commonest neurological manifestation in 85.7% of the cases as reported by Seneviratne and Dissanayake, followed by ophthalmoplegia (75%), limb paresis (26.8%), respiratory failure (17.9%), palatal weakness (10.7%) and weakness of neck muscles (7.1%)**[26]**. A study by Shivali Panwar et al reported neuroparalytic features, and ptosis was presented in majority of the patients (50.9%) followed by ophthalmoplegia (44.9%), difficulty in breathing (28.9%) and muscle weakness (23.1%).**[25]** Most cases admitted to my institution presented with neuroparalytic features, and ptosis was presented in majority of the patients (78.26%) followed by ophthalmoplegia (69.54%), difficulty in breathing (65.21%) and muscle weakness (65.21%). Two patients having no definitive history of pain in patients with neuroparalytic features. So, predominance of neurotoxic features combined with painless bites in our study suggested predominance of krait envenomation. Similarly, Chauhan et al. reported increased incidence of neuroparalytic envenomation in North India and haematotoxic envenomation in South India**[27]**. The hemolytic manifestations of snake envenomation were common in bites caused by the Viper family. These manifestations were persistent oozing from the bite mark, epistaxis, haematemesis, hemoptysis and cutaneous ecchymoses. Mehta et al. reported subconjunctival, retroperitoneal and intracranial haemorrhage following snake bite[28]. However, in our study, 5 patients presented with epistaxis along with neuroparalytic features and these 5 patients progressed to acute renal failure requiring dialysis. Krait bites are more common during the night whereas cobra and viper bites are more common in the day time**[29]**, and similar observation in my study re-enforces the fact that Cobra was the predominant cause of snake envenomation.

ASV is definitive treatment of snake envenomation, and intensive care in the form of ventilator support might be required for patients who develop severe neuroparalytic features. In my study, 15 patients developed difficulty in breathing, required mechanical ventilation for a mean period of 4.8 days. Three patients required platelet transfusion and 5 required fresh frozen plasma transfusion in the ICU. Five patients developed oliguria and progressed to acute renal failure requiring dialysis treatment. Cardiac arrest occurred in three patients while transferring to ICU, CPR was given but developed Hypoxic Brain Injury. The mortality was 30.43% (7) patients and out of these 7 patients, 4 died due to acute renal failure with DIC. Three patients who were referred from medicine ward, cardiac arrest occurred while transferring to ICU and develop Hypoxic brain Injury, deteriorated further in the ICU and died. There was no case fatality in those patients who were treated with anti-snake venom early. Increased complications and mortality was seen in patients who presented after three hours of snake bite and received anti-snake venom late. The toxin present in cobra (cobratoxin) and krait venom (bungarotoxin) binds to the acetylcholine receptors on the post synaptic motor end plate[30]. Anti-snake venom acts by neutralizing the effects of snake venom in the circulation. ASV should be administered as early as possible in symptomatic envenomation as snake venom which has been already bound to the target receptors is not neutralized by the effects of anti-snake venom. The average dose of ASV in my study was 10 vials per patient. Only two patients required higher dose of ASV. It has been reported that neuroparalytic snake envenomation requires higher doses of ASV as compared to hemotoxic envenomation[31]. Raina et al[21] used a mean dose of (292.6±196.27) mL (range 50-950 mL) in the management of snake envenomation. Agarwal et al[32] have used high doses of ASV with median dose of ASV 90 vials (40-140 vials) for neuroparalytic snake bites. The WHO guidelines recommend an initial trial with anticholinesterases for patients of neurotoxic envenomation. The trial would continue if patients show improvement in the neurotoxic symptoms. Anticholinesterases can improve symptoms of patients with bite from cobra envenomation and krait (bungarotoxin), which act post synaptically. However, the predominant action of krait venom is presynaptically (bungarotoxin)[33] and prevents the release of acetylcholine at the neuromuscular junction. Therefore, treatment with anticholinesterase drugs might not improve symptoms in some patients of krait envenomation. As most patients in our study presented with neurotoxic symptoms, we administered neostigmine 0.5 mg twice hourly and atropine to all the patients and observed them closely for clinical improvement.

As neuroparalytic symptoms are predominant in the study, we presumed the bites to be cobra and krait. Majority of the patients in our study had history of working in day time, so we presumed that majority

of the bites were caused by cobra, and two presented with early morning neuroparalytic features and painless bites and required higher dose of ASV and longer ventilation, which were presumed to be bitten by the krait. However, we could not confirm as many patients did not give a positive history of seeing the snake or give a proper description of the snake. There were no snake venom detection kits in this hospital to confirm the presence of venom in the blood or identify the species of the snake. Five patients presented with haematological manifestation were presumed to be bitten by Russell's viper. A 20 minute whole blood clotting test was done for all patients. Special investigations like D dimers, fibrin degradation products and serum fibrinogen levels were not done in all the patients during the ICU period. Another limitation of our study is that a large number of patients with snake bite are treated through traditional healing methods in Bangladesh and might not turn to the ICU. This might lead to an unwanted bias in our study as it might not reflect the true incidence in the community.

Conclusion

In conclusion, the study has showed that early administration of ASV and respiratory support could prevent the death of neurotoxic snake envenomation. There is a need to educate the masses and healthcare providers about the identification of neuroparalytic symptoms and treatment with ASV administration to avoid fatal complications, as always. Neuroparalytic Cobra envenomation is accounted for the highest incidence of venomous bites in the present study. Early medical treatment with judicious anti snake venom administration, mechanical ventilator support and related education is crucial.

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